

## REMARKS

Applicants respectfully request reconsideration of the present application in view of the reasons that follow.

### I. Status of the claims

Claims 8 and 14 were previously cancelled without disclaimer or prejudice. Claims 1, 14, and 15 are amended presently.

Claim 1 is revised to recite a temperature of “at least 45°C.” Exemplary support for this amendment is found in the priority document at pages 2 and 8, and in the present specification at page 9, line 4.

Amended claims 14 and 15 recite an “adsorbent volume [that] is determined from the packed bed height (Ho) of the adsorbent at rest.” Exemplary support is found throughout the specification, for example, at page 10, line 35, at page 20, lines 26 and 27, and in the priority document at page 9, lines 23 and 24, and at page 19, line 9 and 10.

Applicants acknowledge that these changes are proffered after a final action on the merits. Yet, because the amendments place the claims in condition for allowance or at least in better condition for appeal, their entry is appropriate and, therefore, is respectfully requested.

Upon such entry, claims 1-7, 9-13 and 15-17 will be pending and under examination.

### II. Claim interpretation

The examiner raises a number of issues in this section of the Office Action. Applicants believe that this issue in general arise from a misunderstanding or misinterpretation of certain data, chromatographic principles, and claim language. In pressing this theme, applicants address each of the examiner’s concerns in turn.

Linear flow rate: columns in parallel

The examiner asserts that the linear flow rate calculations presented in the reply dated December 19, 2010 (“the 2010 reply”), are incorrect with respect to the experiment described in Example 19 at pages 44-45 of WO 02/096215. Specifically, the examiner contends that the columns described in Example 19 at pages 44-45 of WO 02/096215 are positioned in series rather than in parallel. Office Action at page 3. Based on this factual assertion, which is inaccurate, the examiner contends that the applicants’ linear flow rate calculations are wrong. Office Action at page 3.

To illuminate the error in the examiner’s assertion, applicants provides an accompanying Declaration under 37 C.F.R. § 1.132 by Mr. Allan Otto Fog Lihme. Mr. Lihme is named as an inventor both on the present application and on WO 02/096215.

In paragraph 6 of his declaration, Mr. Lihme attests that the columns described in the Example 19 of WO 02/096215 are positioned in parallel and not in series; further, Mr. Lihme attests, at paragraph 10 of his declaration, that “the knowledgeable reader of WO 02/096215 would appreciate that …the columns were arranged in parallel and the flow rates were much lower than 1500 cm/hr.”

Applicant will not repeat here Mr. Lihme’s technical commentary on the basis for the foregoing attestations. It is apparent, nevertheless, that his statements quoted above are not conclusory but rather convincingly contravene the examiner’s rationale for rejection. See, e.g., paragraphs 4-10 of Mr. Lihme’s declaration. At this juncture, therefore, the examiner has the obligation to explain, clearly and specifically, his disposition of the declaration evidence, pro or con. See MPEP § 716.01, section B.

Independence of cross-sectional area

At the bottom of page 3 and continuing to page 4 of the action, the examiner also expresses a perspective that is erroneous with respect to how linear flow rate is independent of cross-sectional column area, whereupon the linear flow rate must be calculated from the cross-sectional area. This is explained, quite simply, as follows. First, one carries out a chromatography on a first column,

noting the cross-sectional area and volume flow rate. The linear flow rate can then be calculated from this first chromatography. If this chromatography is repeated in a different column of known cross-sectional area, then the required linear flow rate is known and can be achieved by balancing volume flow rate against column diameter.

Claims 15 and 17

Regarding claims 15 and 17, the examiner continues to urge that the “flow rate” recited in claim 1 must be broadly interpreted in order to encompass the language of claims 15 and 17 (e.g., where “the volume applied per litre of adsorbent in one hour is at least 50 l” or “the volume applied per litre of adsorbent in one hour is at least 100 l”). See the Office Action at page 4, for instance, continuing to page 5. The examiner’s misunderstanding and misinterpretation of the claim language is made clear by his statement: “[i]t is unclear how any description having volume applied per hour is not perceived as something else other than flow rate.” Office Action at page 4. While the examiner correctly states that the phrase “in one hour” cannot be ignored in claims 15 and 17, he fails to account for “per liter adsorbent” in the asserted claim interpretation; thus the confusion.

Claims 15 and 17 relate to the volume of fluid *per liter of adsorbent per hour*. These claims fall within the scope of claim 1 when the volume of adsorbent is high. In that claims 15 and 17 depend from claim 1, they should be interpreted in a manner consistent with claim 1, not the other way around.

In addition, in the sentence bridging pages 4 and 5 of the action, the examiner advances an incorrect calculation: if the volume of claim 15 is applied onto 2 liters adsorbent, then the volume of liquid that must be applied to 2 liters of adsorbent to fulfill the claim in fact is 100 liters ( $100/2 = 50$ ), not 25 liters as the examiner has asserted.

Expansion of the adsorbent

The examiner also asserts, *e.g.*, at page 5, lines 2-10, at that EBA adsorbent volume expands and contracts as the flow rate changes, which allegedly is relevant to claims 15 and 17. This is another incorrect assertion, however.

The skilled artisan would understand that the volume of adsorbent in an EBA column is determined from the packed / sedimented bed height ( $H_0$ ), of the adsorbent bed at rest (no flow). When adsorbent volume is measured, the adsorbent is fully hydrated in aqueous buffer, prior to running the column. This is illustrated in Examples 6-9 and 11-13, in which the height of the bed and the diameter of the column are directly provided at hydration and packing. See also page 10, line 35, which describes  $H_0$  as “the height of the bed in packed bed mode (without flow).” Accordingly, this value (the volume of adsorbent) remains a constant for a given packed column.

As the examiner correctly notes, the *bed height* of an EBA column may change as a function of the flow rate. This is recognized in the present application as well, *e.g.*, in paragraph [0067]. Yet, the adsorbent particles themselves do not change their volume (*i.e.*, the particles do not swell or shrink). The only change is the distance between the particles/ beads.

Solely to expedite prosecution and without acquiescing to the examiner’s assertions, claims 15 and 17 have been amended to recite “wherein the adsorbent volume is determined from the packed bed height  $H_0$  of the adsorbent at rest.”

**III. Priority**

The examiner asserts that the priority document PA 2003 00443 does not support the recited temperature range of “at least 50°C.” In particular, the examiner contends that the priority documents discloses a temperature range of “between 45°C to 80°C” and “between 50°C and 70°C” and that this disclosed range does not support the temperature range recited in the claims. Thus, the examiner concludes that the present claims have priority date of March 19, 2004, the filing date of PCT/DK04/00187, and not the filing date of PA 2003 00443, which is March 21, 2003. Applicants are obliged to challenge this assertion, too.

As a preliminary matter, the priority document includes two different page numbers; a page number at the top of each page and one at the bottom. The bottom page number takes into account the cover page of the document and thus is one number higher than the number at the top of each page. As the examiner appears to have referenced the top page number, applicants will follow suit in this reply.

Without conceding to the examiner's assertions and solely to expedite prosecution, claims have been amended to recite "at least 45°C." Support for this amendment is found in the priority document at page 8 (top page number) lines 4-5, which states as follows: "In currently interesting embodiments of the invention, the chromatographic column is operated at temperatures of at least 45°C." Accordingly, priority to PA 00443, with filing date of 3/21/2003 is proper.

#### IV. Claim rejection – 35 U.S.C. § 102(b)

##### A. Lihme

Claims 1-7, 9-13 and 15-17 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by WO 02/096215 ("Lihme"). Applicants traverses this ground of rejection. Contrary to the examiner's assertion, Lihme does not disclose isolating biomolecules via a method that employs both high linear flow rates and high temperatures, as recited in the claims.

This anticipation rejection appears based on the erroneous assertion that Lihme discloses a working example of chromatographic methodology that employs a linear flow rate "exceed[ing] the linear flow rate of 1500 cm/hr" and that also is performed at a high temperature. Office Action at page 7. In particular, the examiner again incorrectly states that, "regarding the calculation of linear flow rate, the Lihme's flow rate exceed[s] the linear flow rate of 1500 cm/hr, in the Example 11 of Lihme et al," that the Lihme "Example 11 also teach[es] temperature of 50°C," and that the "recited flow rate of '1500-3000 cm/hr' would be prophetic linear flow rate if said flow rate are not enabled...however, it is clearly enabled as Lihme...has demonstrated liner [sic] flow rate of 1628 cm/hr." Office Action at page 7.

In the first instance, Example 11 clearly states that “[t]he whey was loaded with a linear flow rate of 7.5 cm/min.” Lihme at page 36, line 16, emphasis added. This is equivalent to a linear flow rate of only 450 cm/hour, less than half the recited flow rate. It is unclear to applicants how the examiner interprets 7.5 cm/min to read on “at least 1500 cm/hr.”

Second, although Example 11 does indeed disclose sample loading at 50°C, as explained above, the linear flow rate in Example is only 450 cm/hr. Thus, the method disclosed in Example 11 *does not* anticipate the pending claims.

Third, Lihme does not demonstrate a liner flow rate of 1628 cm/hr, as the examiner contends. Example 19 utilizes a *parallel*, two- or three-column system, as discussed above and as Mr. Lihme attests. The linear flow rates in this example are not “at least 1500 cm/hr,” but instead are “much lower than 1500 cm/hour.” Lihme Dec. at ¶ 10.

In support of this conclusion, the examiner emphasizes to applicants that “[a]ccording to ‘MPEP 2136.02 ...REJECTION MAY RELY ON ANY PART OF THE PATENT OR APPLICATION PUBLICATION DIS-CLOSURE.’” Office Action at page 7 (emphasis in original). Applicants do not take issue with the substance of this citation – merely its relevance. It is unclear exactly which part or parts of the Lihme reference would support an anticipation rejection, given that Lihme does not disclose a chromatographic method with the recited linear flow rates and the recited high temperatures.

Accordingly “the identical invention is not shown in as complete detail as is contained in the claims,” nor are the elements “arranged as required by the claim.” MPEP § 2131, citing *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1239, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989), and *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990). It necessarily follows that the present claims are not anticipated by Lihme. Reconsideration and withdrawal of this rejection are requested, therefore.

B. Flickinger

Claims 1, 3-7 and 9-13 are rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,837,826 to Flickinger (“Flickinger”). Applicants respectfully traverse this ground for rejection. Flickinger does not provide an enabling disclosure of the claimed methods.

In particular, Flickinger does not disclose a fractionation method at high linear flow rate (at least 1500 cm/hr) *and* at high temperature (at least 45°C). Indeed, as detailed in the previous reply dated 12/9/2010, it is highly probable that a column as disclosed in Flickinger run under the high flow rates and high temperatures prescribed in the claims would be non-functional (*i.e.*, not enabled). As such, Flickinger cannot anticipate the pending claims.

In the Office Action, the examiner dismisses applicants explanations regarding the problems of running Flickinger’s columns at 4000 cm/hr, and asserts that “[t]he method of Flickinger ... would be hypothetical if the disclosure was not enabled; however it has been determined that it is enabled at the time of instant invention as instant office action lacks scope of enablement rejection under 35 USC 112, first paragraph.” Office Action at page 10. This statement is exceedingly unclear; however, applicants assume the examiner’s point to be that since Flickinger is a granted patent, the full scope of all claims is presumed valid, and thus, enabled. In support of this assertion – whatever its true meaning – the examiner emphatically repeats the following statement: “[a]ccording to ‘MPEP 2136.02 ...REJECTION MAY RELY ON ANY PART OF THE PATENT OR APPLICATION PUBLICATION DIS-CLOSURE.’” Office Action at page 10, emphasis in original.

Irrespective of the status of Flickinger as a patent, applicants submit that Flickinger, as a whole - or “any part” thereof - *does not enable* the claimed subject matter. Flickinger provides prophetic ranges of high linear flow rate, but as discussed in the previous reply and as attested by Mr. Allen Otto Fog Lihme, such flow rates are *not* enabled.

As Mr. Lihme attests, “I ... believe it is highly *unlikely* that the columns described in Flickinger could operate effectively, if at all, were they run at the flow rates and temperatures that

characterize the invention of the application...*without substantial modification.*” Lihme Dec. at ¶¶ 12 and 15 (emphasis added). With respect to such modification, Mr. Lihme describes that “the parameters and variables in EBC are complex and interlinked,” and that “I and other in the EBC area would be obliged to carry out an *extensive program of research* to balance the relevant parameters to increase flow rates from a known ‘high’ working rate (e.g., 220 cm/hr) to the much higher rate of 1500 cm/hr.” Lihme Dec. at ¶ 14. Mr. Lihme further attests that “[w]hich variables or parameters to change and precisely how to change them are not subject to a foregone conclusion with any EBC system,” and that “[i]ncreasing flow rate, especially to rates greater than 1500 cm/hr in an EBC system, is not simply a matter of ‘opening the tap.’” Lihme Dec. at ¶ 14.

The “disclosure in an assertedly anticipating reference *must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient*, if it cannot be produced without undue experimentation.” MPEP § 2121.01 (citations omitted; emphasis added). Applicants respectfully submit, in concert with Mr. Lihme’s attestations, that Flickinger does not provide an enabling disclosure for a high temperature and high linear flow rate chromatography method as recited in the pending claims.

Accordingly, Flickinger does not anticipate the pending claims, and withdrawal of the rejection under 35 U.S.C. § 102(b) is requested.

**V. Non-statutory obviousness-type double patenting**

Claims 1-7, 9-13 and 15-17 are rejected on the grounds of non-statutory obviousness-type double patenting. Specifically, the examiner asserts that claims 1, 3-5, 7-16, 19-23 and 27-33 of U.S. Patent No. 7,812,138 render the pending claims obvious in light of the teachings of Lihme and/or Olander *et al.*, SCANDINAVIAN DAIRY INFORMATION 2, 22-25 (Orlander).

These claims also are rejected for obviousness-type double patenting over claims 1-23 and 26-28 of U.S. patent No. 7,368,141, claims 18-31 of U.S. patent No. 6,783,962, claims 1-15 of U.S. patent No. 6,498,236, or claims 1-6 of U.S. patent No. 6,620,326, all in view of Lihme and/or Olander.

Applicants respectfully traverse these grounds for rejection. Each of the rejections is founded on an erroneous understanding of the Lihme reference and the flow rates disclosed there. As detailed in sections II and IV and as attested by Mr. Lihme in his declaration, the Lihme reference does not disclose isolation methodology employing both the high linear flow rates and the high temperatures recited in the pending claims.

Applicants further submit that none of the cited claims cited recites or conveys *both* “a linear flow rate of at least 1,500 cm/hour” *and* a “temperature of at least 45°C.” Accordingly, the allegation of obviousness has no merit, and these obviousness-type double patenting rejections should be withdrawn.

## CONCLUSION

Favorable reconsideration of the application is respectfully requested. Examiner Kim is invited to contact the undersigned directly, should he feel that any issue warrants further consideration.

Respectfully submitted,

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